Urinalysis
Interpretation and Clinical Correlations

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KEYWORDS

• Urinalysis • Proteinuria • Hematuria • Glucosuria • Ketonuria • Crystalluria
• Nephrolithiasis

KEY POINTS

- Urinalyses are commonly ordered and widely available, and are a powerful tool to help understand potential pathologies related to the kidney and urinary systems.
- Urine samples have several physical and chemical properties that can be relevant to clinical scenarios.
- Urine microscopy can reveal evidence of conditions including glomerular disease, intrinsic kidney injury, nephrolithiasis, or drug-induced crystalluria.
- Concomitant urinalysis with bloodwork is a key initial step in diagnosing glomerular diseases.

INTRODUCTION

Urinalysis is an invaluable, noninvasive diagnostic test that is commonly used in clinical practice in both inpatient and ambulatory settings. Correct interpretation of urine studies in conjunction with a patient's history, physical examination, and laboratory data can provide clinicians with crucial information about a wide variety of primary kidney and systemic disorders, even in asymptomatic patients.[1,2] This review serves to summarize the interpretation of various patterns of urinalysis findings. We aim to aid primary care and internal medicine physicians in using urinalysis to (1) evaluate suspected acute and chronic kidney diseases, (2) monitor the course of established diseases, and (3) refine the differential diagnosis and optimize further workup in settings of unknown disease pathology.

DEFINITIONS

- Spot urine collection: a small sample of urine from a single voiding event
- Timed urine collection: a sample of urine collected from multiple voiding events over a specified time period (typically 24 hours)

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- Urine microscopy: examination of urine elements under a microscope to detect the presence of various cells, casts, and crystals
- Proteinuria: the presence of elevated levels of proteins in the urine, which can include albumin as well as other serum proteins such as globulins
- Albuminuria: the presence of elevated levels of albumin in the urine
- Acute kidney injury (AKI): increase in serum creatinine by $\geq$0.3 mg/dL within 48 hours, increase in serum creatinine by >1.5$\times$ baseline, or urine volume <0.5 mL/kg/h over a 6-hour period[3]
- Chronic kidney disease (CKD): persistently impaired estimated glomerular filtration rate <60 mL/min/1.73 m^2 or persistently elevated urine albumin excretion $\geq$30 mg/g creatinine, or both, for more than 3 months[3]

When Should Urinalysis Be Pursued?

Urinalysis is a simple and inexpensive test that can be performed in many clinical situations. There is currently insufficient evidence to support universal urinalysis screening.[4–6] We recommend urinalysis for the following patients.

1. Any patient with an elevated serum creatinine level, in the evaluation of either AKI or CKD
2. Patients with diabetes, hypertension, or cardiovascular disease[7,8]
3. Patients with new or unexplained progressive edema
4. Patients being evaluated for certain systemic diseases with renal manifestations, such as lupus, vasculitis, or monoclonal gammopathies
5. Patients presenting with symptoms or clinical evidence of nephrolithiasis
6. Patients with concerns of discolored urine, frothy urine, or symptoms consistent with urinary tract infections (UTIs)

How Should a Urine Specimen Be Collected?

In most clinical situations, investigation of urine begins with a spot collection. Proper collection and handling of urine specimens is important to maximize the diagnostic yield and achieve reliable interpretation of findings. Midstream clean-catch collections are preferred to reduce cellular and microbial contamination from skin flora. Early morning samples are optimal, as urine accumulated overnight is more concentrated and contains relatively higher levels of cellular elements and proteins, which can be missed in dilute samples.[9] Early morning samples can also provide more reliable information about a patient's urine concentrating capacity.

During evaluation of specific conditions such as glomerular disease, monoclonal gammopathies, or nephrolithiasis, collection of 24-hour urine samples may be warranted. Patients should be instructed to discard their first morning void and subsequently collect all urine produced over the following 24 hours.[10]

In patients with an indwelling urinary catheter, fresh samples should be taken from the side port of the catheter, as this represents recently produced urine. Samples taken from collection bags can be affected by precipitation and contamination and are considered inaccurate. If a patient is undergoing evaluation for a possible UTI, indwelling catheters should first be replaced, with a urine sample and culture sent from the fresh catheter.[11]

Samples from patients with nephrostomy tubes should ideally be obtained at the time of tube placement. For patients who already have a nephrostomy tube in place, the drainage bag should be changed, and a subsequently produced urine sample should drain by gravity into a sterile collection container. Urostomy samples are recommended to be collected by transiently catheterizing the stoma and collecting the

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first subsequent void. Specimens should not be collected from the urostomy pouch or drainage bag, as both will contain significant contamination.[12,13]

How Should Specimens Be Handled?

Once a spot sample is collected, urinalysis should be performed within 2 to 4 hours, as delays between collection and examination can influence results due to instability of some urinary components and overgrowth of clinically significant or contaminating flora.[14,15] Samples processed outside of this timeframe may be affected by alterations in cellular morphology and the development of cellular casts or crystals that have developed ex vivo. If a specimen cannot be examined promptly, such as a 24-hour timed urine collection, it should be refrigerated at a temperature of 2°C to 8°C for 24 to 48 hours.[16,17] Storage at cold temperatures can still result in some inaccuracies due to decomposition and/or precipitation of phosphates and urates.

What Methods Can Be Used to Analyze a Urine Sample?

A urinalysis, also referred to as a urine dipstick test, uses a plastic strip with attached chemical reagent pads for pH, protein, glucose, ketone, bilirubin, urobilinogen, blood, nitrite, and leukocyte esterase. The dipstick can be analyzed manually based on visual color changes to the various reagent pads, or placed into an automated reader, which is the standard for a urinalysis examination in a clinical laboratory. This testing method comes with some limitations stemming from common false-positive and false-negative results.[18] A urine microscopy test to visualize cells, casts, and crystals is typically done as a secondary test when abnormalities are found on the initial urinalysis.

What Are the Commonly Reported Properties of Urine?

A urinalysis consists of three components (**Table 1**): physical properties, chemical properties, and elements identified by microscopic examination.[18–20] Each of these components can provide unique insight into the pathology of a patient's kidney or urologic conditions.

- Color: Normal urine is clear with a light/pale yellow tinge due to the presence of urochrome generated from heme breakdown. Urine color can be affected by a

Table 1
Properties of urinalysis

Physical examination	Color Odor Turbidity Specific gravity
Chemical examination	pH Protein Glucose Urobilinogen, bilirubin Ketone bodies Leukocyte esterase Nitrites
Microscopic examination	Cells Casts Crystals Microorganisms

Characteristics obtained from physical, chemical, and microscopic examinations are listed.

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variety of normal or pathological conditions, metabolic products, medications, foods, drugs, and infections[18–25] (**Table 2**).

- Odor: Urine odor can be altered by certain clinical conditions, foods, bacteria, and drugs[18–20] (**Table 3**).
- Turbidity: While urine is normally clear or transparent, turbidity can be reported in settings of crystal precipitation after refrigeration, or with the presence of erythrocytes, blood clots, leukocytes, bacteria, squamous epithelial cells, vaginal secretions, semen, or chyluria.[18–20]
- Volume: In adults, urine volume ranges from 600 mL to 2000 mL over 24 hours, on average. Patients with <100 mL of urine per day are deemed anuric, whereas oliguric patients produce <500 mL/day. Polyuria is suspected when urine output exceeds 3000 mL over 24 hours in adults and can be seen in conditions such as diabetes mellitus, diabetes insipidus, psychogenic polydipsia, diuretic use, or excess alcohol or caffeine consumption.[26,27] In the nonacute setting, 24-hour urine volumes can be useful to objectively assess for polyuria or to determine if hydration status might be a contributing risk factor for nephrolithiasis.
- Specific gravity (s.g.): The urine s.g. measures the concentration of solutes (number and size of particles) in urine. The range is dependent on the amount of fluid ingested and solute excreted. If urine does not contain glucose, proteins, or large molecules such as contrast media, the urine osmolality can be inferred from urine s.g. (urine s.g. of 1.001–1.035 corresponds to urine osmolality of 50–1200 mOsm/kg). Indirectly, urine s.g. can provide information on urinary concentrating and diluting capabilities and can be helpful in evaluation of volume disorders, as well as disorders of water balance such as hyponatremia or hypernatremia.[28]
  - High urine s.g. is seen in cases of volume depletion, syndrome of inappropriate antidiuretic hormone, and glucosuria. It can also be induced with administration of hyperosmotic solutions including iodinated contrast, IV albumin, and dextran.
  - A urine s.g. of 1.010 is isotonic to plasma (isosthenuria).
  - Urine s.g. <1.010 indicates urinary dilution and can be seen in conditions including excessive fluid intake, psychogenic polydipsia, and diabetes insipidus. A urine s.g. $\leq$1.003 indicates maximally dilute urine.
- Urine pH: Urine pH reflects the degree of acidification of urine. Physiologic urine pH ranges from 4.5 to 8 depending on systemic acid-base balance. On a typical Western diet, urine is slightly acidic (pH 5.5–6.5) because of metabolic activity, which predominantly favors acid formation. Determination of urine pH is useful in the diagnosis and management of nephrolithiasis, metabolic acidosis, and UTIs (**Table 4**) and provides insight into tubular function. Low urine pH can be seen in patients with high-protein diets, systemic acidosis, type IV renal tubular acidosis (RTA), and heavy intake of certain fruits and medications (eg, cranberries ormethionine). High urine pH can be seen in patients following a strict vegetarian diet, patients with systemic alkalosis, UTIs caused by urease-producing organisms, or type I RTA.[19] Changes in urine pH may also be helpful in management of drug toxicities requiring urinary alkalinization, such as methotrexate, salicylate, phenobarbital, and chlorpropamide toxicity.[29]
- Hematuria: Hematuria can be gross (visible to the naked eye) or microscopic (detectable only on urinalysis). Microscopic hematuria refers to the presence of 3 or more erythrocytes per high-powered field.
  - Dipsticks are very sensitive to urinary hemoglobin, which can be free or seen within red blood cells (RBCs). Dipsticks detect the peroxidase activity of erythrocytes, which is also catalyzed by myoglobin and hemoglobin; therefore, a positive test result may indicate hematuria, myoglobinuria, or hemoglobinuria.

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Table 2
Urine color

Color	Conditions	Drugs/Substances	Foods
Dark yellow	Concentrated urine in dehydration or exercise	Vitamin preparations, rifampin	Carrots
Pink/red	Hematuria, hemoglobin, myoglobin, porphyrin, massive uric acid crystalluria	Phenothiazines	Beets, blackberries, rhubarb
Orange	Bilirubin, bile pigments	Phenazopyridine, vitamin C, rifampin, phenothiazines, warfarin	Carrots
Green/blue	*Pseudomonas* UTI	Cimetidine, propofol, amitriptyline, biliverdin, promethazine (Phenergan), triamterene, cimetidine, methylene blue, and indigo dyes	Asparagus
Purple	Infection with *Escherichia coli* or *Pseudomonas*, bacteriuria from indwelling catheter	Hydroxocobalamin	
Black/brown/tea colored	Bile pigments, myoglobinuria, methemoglobin, melanuria, porphyria, homogentisic acid (alkaptonuria)	Chloroquine, levodopa, methyldopa, nitrofurantoin	Rhubarb
Cloudy/white	Pyuria, chyle, calcium phosphate crystals, struvite crystals	Propofol	

Conditions, drugs, substances, and foods associated with different urine colors are shown.[18–25]

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Table 3
Urine odor may be affected by a variety of substances or conditions, as shown[18–20]

Odor	Substances or Conditions
Strong smell	Concentrated urine, dehydration, old specimen
Fruity or sweet odor	Acetone in diabetic ketoacidosis
Ammoniac	Alkaline fermentation after prolonged bladder retention, UTI by urease-producing organisms
Pungent	UTI, asparagus consumption
Fecal	Gastrointestinal bladder fistula
Burnt sugar/maple syrup	Maple syrup urine disease
Mousy/musty odor	Phenylketonuria
Sulfur	Asparagus, sulfa medications

Microscopic examination of the urine sediment is the gold standard for detection of hematuria and may also identify RBC casts or dysmorphic RBCs.

- Hematuria is divided into glomerular, nonglomerular, and urologic etiologies.
  - Glomerular hematuria can be associated with dysmorphic RBCs, erythrocyte casts, and proteinuria, and can be seen in conditions such as IgA nephropathy, type IV collagen diseases, thin basement membrane disease, or various nephritic diseases. Patients with glomerular hematuria should be referred to nephrology for further evaluation.
  - Nonglomerular hematuria can be associated with proteinuria, without dysmorphic RBCs or erythrocyte casts. Nonglomerular hematuria can be seen in patients with tubulointerstitial disease, polycystic kidney disease, sickle cell disease, or papillary necrosis. A subclass of nonglomerular hematuria is urologic hematuria, which can be associated with passage of clots. Patients with urologic hematuria should be referred for further evaluation of etiologies such as nephrolithiasis, malignancies, benign prostatic hyperplasia, or lower UTIs.[30]

- Proteinuria: Proteinuria is a very common finding and can arise from several different physiologic and pathologic causes. The presence and degree of proteinuria, especially albuminuria, is important for CKD staging and the prognostication of progression.[31,32] Proteins <20,000 Da pass easily across the glomerular capillary wall; however, the negatively charged large protein albumin (69,000 Da) is repelled by the glomerular capillary wall and normally present in only small

Table 4
Analysis of urine pH

Nephrolithiasis	• Urine pH < 5.5: uric acid stones • Urine pH > 6.5: calcium phosphate stones
Metabolic acidosis	• Urine pH < 5.5: Type IV RTA (hyperkalemic distal RTA) • Urine pH > 5.5: Type I RTA (hypokalemic distal RTA) • Type II (proximal) RTA initially results in alkaline urine due to an inability to reabsorb bicarbonate, but urine later becomes acidic as the filtered load of bicarbonate decreases.
UTIs	• Urine pH > 7.0: UTI secondary to urease-producing organisms

Urine pH can guide evaluation of conditions including nephrolithiasis, metabolic acidosis, and UTIs.
Abbreviation: RTA, renal tubular acidosis.

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amounts in glomerular filtrate.[32] Most smaller-molecular-weight filtered proteins are largely reabsorbed and metabolized primarily in proximal convoluted tubules, with only small amounts excreted. Tamm-Horsfall glycoprotein is secreted by tubular cells and comprises 40% to 50% of total urinary proteins, with the rest being primarily made of albumin and globulins.

- Some patients may experience transient proteinuria, which can occur due to temporary changes in glomerular hemodynamics and usually resolves as the precipitating factor is addressed. Some causes of benign transient proteinuria are dehydration, exposure to extreme heat or cold, emotional stress, fever, inflammatory processes, UTIs, acute illnesses, vaginal mucus, heavy exercise, or orthostatic changes (postural proteinuria).
- On the other hand, persistent proteinuria or albuminuria suggests the presence of kidney disease and can be divided into three categories[32,33]:
  - Glomerular proteinuria is the most common cause of proteinuria and occurs as a result of altered permeability of a damaged glomerular basement membrane, causing urinary loss of large-molecular-weight proteins such as albumin and immunoglobulins. In many cases, glomerular proteinuria is further quantified by assessing albuminuria, which is classified into three stages[34]: A1 (less than 30 mg/g creatinine; normal to mildly increased), A2 (30 mg/g to 300 mg/g creatinine; moderately increased, "microalbuminuria"), and A3 (greater than 300 mg/g creatinine; severely increased, “macroalbuminuria”).
  - Tubular proteinuria results from an inability of malfunctioning tubular cells to metabolize or reabsorb normally filtered low-molecular-weight proteins (eg, retinol-binding protein, α-2-microglobulin, β-2-microglobulin). Tubular proteinuria is typically <2 g/d.
  - Overflow proteinuria occurs when low-molecular-weight proteins (eg, myoglobin, immunoglobulin light chains) are overproduced, thereby overwhelming the ability of the tubules to reabsorb all filtered proteins.
- Proteinuria can be further classified as subnephrotic range (150–3000 mg per day) or nephrotic range (>3500 mg per day). This classification helps narrow potential disease etiologies (**Table 5**).

Table 5
Potential disease etiologies by degree of proteinuria

Nephrotic range proteinuria (>3500 mg/d)	• Diabetic nephropathy • Focal segmental glomerulosclerosis • Minimal change disease • Membranous nephropathy • Amyloidosis • Dysproteinemia (eg, multiple myeloma)
Subnephrotic proteinuria (150–3000 mg/d)	• IgA nephropathy • Type IV collagen diseases (eg, thin basement membrane disease) • Lupus nephritis • Infection-related GN • Membranoproliferative GN • Anti-GBM disease • ANCA vasculitis • Acute interstitial nephritis

Several disease etiologies can present with variable proteinuria levels.
Abbreviations: GBM, glomerular basement membrane; GN, glomerulonephritis; ANCA, antineutrophilic cytoplasmic antibody.

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- Nephrotic range proteinuria is seen in primary glomerular diseases (eg, minimal change disease or membranous nephropathy), but can also be seen in cases of overflow proteinuria (eg, multiple myeloma). When nephrotic range proteinuria is associated with hypoalbuminemia and edema, it is called nephrotic syndrome. Patients with nephrotic syndrome should be referred for prompt nephrology evaluation.
- Subnephrotic range proteinuria can be seen in settings of glomerular (eg, glomerulonephritis) or nonglomerular parenchymal renal disease (eg, tubulointerstitial or vascular processes).
- Many disease pathologies can present with variable degrees of proteinuria. Regardless, patients with unexplained proteinuria, or progressive proteinuria with hematuria, should be evaluated by a nephrologist.

Proteinuria may be quantified by several different approaches:

- Urine dipstick: A standard urine dipstick test is the most common first-line screening tool for proteinuria. The reagent on most dipstick tests is sensitive to albumin, with 1+ corresponding to 30 mg/dL protein, 2+ to 100 mg/dL, 3+ to 300 mg/dL, and 4+ to 1,000 mg/dL albuminuria. Urine dipstick testing is usually highly specific for detecting proteinuria but has lower sensitivity.[35] False results can occur in situations of varied urine concentration. Positive results may be seen in dehydrated patients with highly concentrated urine, patients who have received iodinated radiocontrast agents, patients who have recently exercised, or patients with gross hematuria, alkaline urine, or a UTI. Very dilute urine can also result in false-negative results.
- Another significant limitation of urine dipsticks is low sensitivity to nonalbumin proteins, such as light chain immunoglobulins and Bence-Jones proteins.[36] This problem can be addressed by performing the sulfosalicylic acid (SSA) test, which is a semiquantitative method available to screen patients for proteinuria. The SSA test reagent detects all proteins in urine including immunoglobulins.[36] When the SSA test is positive with a negative dipstick, it usually indicates the presence of nonalbumin proteins in the urine. As neither dipstick nor the SSA method is quantitative, more formal urinalysis testing should be pursued if one of the described tests is positive.
- Twenty-four-hour urine protein excretion: The gold standard to quantify proteinuria is a 24-hour urine collection, as it eliminates variations in proteinuria associated with the circadian rhythm and can also be standardized to a 24-hour urine creatinine. There are certain limitations to this approach, mostly surrounding methods and difficulty of collection. It can be impractical and cumbersome in outpatient settings or in care of older patients, and is susceptible to overcollection (urine collected for >24 hours) or undercollection (urine collected for <24 hours), which can influence results.
- Spot urine albumin-to-creatinine ratio (UACR) and urine protein-to-creatinine ratio (UPCR): An alternative to 24-hour urine protein excretion is quantification of the UPCR or UACR, both of which use a spot urine sample. UACR and UPCR are more accurate than urine dipsticks and correlate well with 24-hour collections in adults.[37] This approach is also easier for patients and standardizes the protein measurement to the quantity of creatinine in the urine, which helps avoid errors introduced by dilute or concentrated urine samples. Major limitations to UPCR and UACR are overestimation or underestimation of proteinuria in individuals with small or large muscle mass, respectively, as it is influenced by urine creatinine. Correlations of

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Table 6
Cellular elements identified on urine microscopy[41–46]

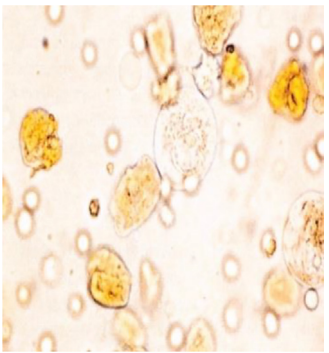
Cell Type	Characteristics	Causes	Representative Image
Epithelial cells	*Renal tubular epithelial (RTE) cells* are larger than PMNs and have a round, large, centrally located nucleus and fine-grained cytoplasm.	Tubular damage, interstitial nephritis	
	Squamous epithelial cells are derived from the distal urethra or external genitalia. They are large and irregular with a small nucleus and fine granular cytoplasm.	Contamination during sample collection	

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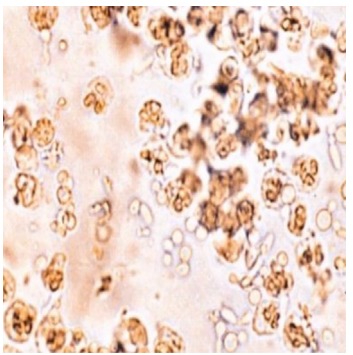
Table 6
(*continued*)

Cell Type	Characteristics	Causes	Representative Image
	Transitional epithelial cells originate from the renal pelvis, ureter, bladder, or proximal urethra. They are smaller and rounder than squamous cells and have larger nuclei.	Contamination during sample collection, transitional cell cancers	
White blood cells[41]	*Neutrophils* are intermediate in size compared with RBCs and renal tubular epithelial cells. They have an agranular cytoplasm and multilobed nuclei.	Urinary tract inflammation or infection, bacteriuria, interstitial nephritis, genitourinary tuberculosis, nephrolithiasis	
	Urine eosinophils can be detected with Wright or Hansel stain to the urine sediment.	Urine eosinophils are found in a variety of kidney diseases. They are not accurate to establish or exclude a diagnosis of acute interstitial nephritis.[42–44]	

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Erythrocytes[45,46]	*Isomorphic RBCs* are small, enucleated cells shaped as biconcave discs.	Nonglomerular hematuria	
	Dysmorphic RBCs have variable shapes because of their passage through the glomerulus. Acanthocytes are RBCs with membrane protrusions.	Glomerular hematuria (52% sensitivity and 98% specificity for diagnosis of glomerulonephritis)	

Images from Primer on Kidney Diseases, Section 1, Chapter 4: Urine analysis and urine microscopy. https://www.sciencedirect.com/book/9781455746170/national-kidney-foundation-primer-on-kidney-diseases#book-info.

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Table 7
Cellular and acellular casts identified on urine microscopy

Casts	Composition	Conditions	Representative Image
Hyaline	Solidified Tamm-Horsfall mucoprotein	Nonspecific; can be seen in concentrated urine from healthy individuals, or in settings of fever, physical exertion, or chronic renal disease	
Erythrocyte	Red blood cells in a tubular cast matrix	Glomerulonephritis, interstitial nephritis; also seen as a normal finding (along with hematuria) in healthy individuals after exercise	
Leukocyte	White blood cells in a tubular cast matrix	Pyelonephritis, interstitial nephritis	

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Epithelial	Renal tubular cells in a tubular cast matrix	Acute tubular necrosis, interstitial nephritis; can also be seen in concentrated urine	
Granular	Fine or coarse casts composed of cellular breakdown products, within a cast matrix	Acute tubular necrosis; also seen in other etiologies such as glomerulonephritis or tubulointerstitial disease	

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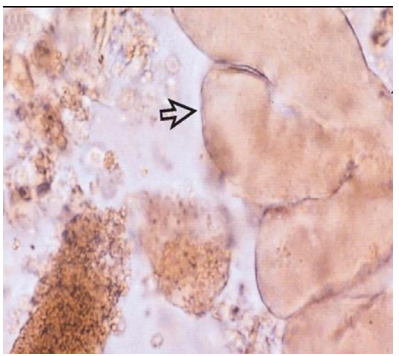
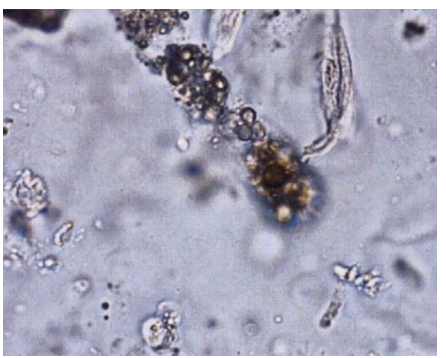
Table 7
(*continued*)

Casts	Composition	Conditions	Representative Image
Waxy	Hyaline material and proteinaceous material	Nonspecific; seen in advanced CKD and AKI	
Fatty	Lipid-laden renal tubular epithelial cells	Nephrotic syndrome	

Images from Primer on Kidney Diseases, Section 1, Chapter 4: Urine analysis and urine microscopy. https://www.sciencedirect.com/book/9781455746170/national-kidney-foundation-primer-on-kidney-diseases#book-info.

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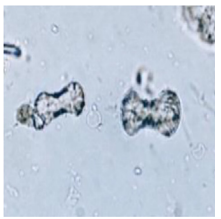
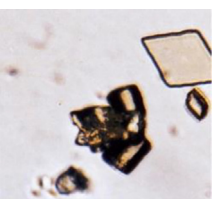
Table 8
Crystals identified on urine microscopy

Type of Crystal	Shape	Urine pH	Associations	Figure
Cystine	Hexagonal shapes similar to benzene rings	Acidic	Cystinuria	
Calcium oxalate	Envelope or dumbbell	Acidic	High dietary oxalate, nephrolithiasis, ethylene glycol ingestion	
Uric acid	Diamond, barrel, rhomboid, or needle-shaped	Acidic, typically with urine pH < 5.5	Urate nephrolithiasis, acute urate nephropathy; less common in normal subjects	
Triple phosphate (magnesium ammonium phosphate)	Coffin lid	Alkaline	Nephrolithiasis, UTIs secondary to urease-producing organisms (*Proteus, Klebsiella*)	

Images from Primer on Kidney Diseases, Section 1, Chapter 4: Urine analysis and urine microscopy. https://www.sciencedirect.com/book/9781455746170/national-kidney-foundation-primer-on-kidney-diseases#book-info.

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spot samples with 24-hour protein excretion are less robust in patients with nephrotic-range proteinuria and in patients who are pregnant.[37]

- Glucosuria: Glucosuria occurs when the filtered load of glucose exceeds the reabsorbing capacity of the tubule, or if the kidney is unable to reabsorb filtered glucose despite normal plasma glucose concentrations.[20] Glucosuria is classically a feature of diabetes and can be seen in Cushing syndrome. Glucosuria in the absence of hyperglycemia suggests proximal tubular dysfunction, which can be seen in multiple myeloma, cast nephropathies, or heavy metal exposure, or due to exposure to certain drugs such as sodium/glucose cotransporter-2 inhibitors, valproic acid, aminoglycosides, cisplatin, and tenofovir.[19]
- Ketonuria: Ketones are products of body fat metabolism. Ketonuria is seen in diabetic acidosis, alcoholic acidosis, starvation, and pregnancy. As the urine dipstick reagent detects the reaction of nitroprusside with acetoacetate and acetone, it underestimates ketone excretion in diabetic ketoacidosis or starvation ketosis, which primarily generate β-hydroxybutyrate.[19]
- Leukocyte esterase: Leukocyte esterase is produced by lysed neutrophils and macrophages and is a surrogate marker for the presence of white blood cells. Proteinuria, glucosuria, ketonuria, and certain drugs such as cephalosporins, nitrofurantoin, tetracycline, or gentamicin can lead to a false-negative leukocyte esterase test. False-positive results are rare but can be seen in contaminated urine samples or in samples mixed with vaginal secretions.
- Nitrites: A positive urine nitrite test indicates the presence of bacteria that are capable of reducing urinary nitrates into nitrites via the nitrate reductase enzyme. Many gram-negative bacteria and some gram-positive organisms (*E. coli*, *Klebsiella*, *Enterobacter*, *Citrobacter*, *Klebsiella*, and *Proteus* species) have this capability. The presence of both leukocyte esterase and nitrites on urine dipstick is highly predictive of a UTI.[38] Urinary infections with species that express low levels of nitrate reductase (*Pseudomonas*, *Staphylococcus*, and *Enterococcus* species) may test negative for nitrites.
- Bilirubin and urobilinogen: Conjugated bilirubin is not normally present in urine in detectable amounts but can be positive in patients with hepatic or biliary

Table 9
Common urinalysis findings with respective likely etiologies

Urinalysis Findings	Likely Etiology
Bland or hyaline casts, few finely granular casts; ± protein	Prerenal azotemia
"Muddy brown" casts, RTE cells or casts; ± protein	Acute tubular injury
Dysmorphic RBCs, RBC casts, subnephrotic proteinuria	Nephritic syndrome
Fatty casts, cholesterol crystals, oval fat bodies, nephrotic-range proteinuria	Nephrotic syndrome
Urine glucose in the absence of hyperglycemia	SGLT2i use; proximal tubular dysfunction from multiple myeloma or cast nephropathies
Urine specific gravity >1.035	Radiographic contrast use; volume depletion
Urine pH > 6 in the setting of systemic non-anion-gap metabolic acidosis	RTA (likely type 1)

Abbreviations: RTE, renal tubular epithelial; SGLT2i, sodium/glucose cotransporter-2 inhibitor.

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Table 10
Common clinical scenarios

Clinical Scenario	Urinalysis Findings	Likely Diagnosis	Next Steps
65-year-old male with a 5-year history of diabetes (A1c 7.5%–9.0%); Cr 1.1 mg/dL	UACR 220 mg/g; UPCR 0.4 g/g	Early diabetic nephropathy	Initiation of RASi, SGLT2i, GLP1-RA; monitoring of albuminuria every 6 mo; nephrology referral with worsening of proteinuria or Cr.
23-year-old male with hematuria and recent respiratory infection; Cr 1.1 mg/dL	3+ blood, 2+ protein; UPCR 1.2 mg/g	IgA nephropathy, postinfectious GN	Nephrology referral (possible kidney biopsy)
32-year-old female with mild anemia and hypercalcemia; Cr 1.3 mg/dL	Dipstick negative for protein, but with ++SSA; UPCR 4.3 g/g; UACR 0.5 mg/g	Dysproteinemia (myeloma, amyloidosis, cast nephropathy)	Nephrology referral (possible kidney biopsy); hematology referral (possible bone marrow biopsy)
75-year-old male with rapid-onset anasarca; Cr 0.9 mg/dL	UPCR 12.2 g/g; UACR 6000 mg/g	Minimal change disease, membranous nephropathy	Nephrology referral (kidney biopsy)
78-Year-old male with 1-mo history of intermittent gross hematuria and blood clots, urinary frequency, nocturia; Cr 1.1	2+ blood on dipstick; no dysmorphic RBCs or RBC casts on urine sediment	Urological malignancy, benign prostatic hyperplasia	Urology referral (cystoscopy)
30-year-old male with 1 episode of transient macroscopic hematuria and flank pain; Cr 1.2	+ blood on dipstick; 10–15 isomorphic erythrocytes on urine sediment	Nephrolithiasis	Noncontrast computed tomography or ultrasound; 24-h urine collection for stone risk panel

Urinalysis findings can help formulate differential diagnoses.

Abbreviations: Cr, creatinine; GLP1-RA, glucagon-like peptide-1 receptor agonists; GN, glomerulonephritis; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium/glucose cotransporter-2 inhibitor.

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obstruction or congenital hyperbilirubinemia.[20] This test is usually negative in patients with jaundice due to hemolysis, as unconjugated bilirubin is fat soluble.

Urobilinogen is the end product of conjugated bilirubin metabolism and is present in urine in only small amounts. Elevated levels suggest an excess of conjugated or unconjugated bilirubin, which can be seen in cases of hemolysis and hepatocellular diseases like cirrhosis and hepatitis. Certain antibiotics (eg, sulfonamides) may produce false-positive results, and exposure of urine samples to daylight or prolonged storage can cause false-negative results due to degradation of urobilinogen.[20]

What Additional Information Is Offered by Urine Microscopy?

Urine microscopic examination is an indispensable part of the evaluation of patients with hematuria, proteinuria, or nephrolithiasis. To perform urine microscopy, a fresh sample of 10–15 mL of urine is centrifuged for at least 5 minutes at >1500 rpm. The supernatant is then poured out, and the sediment is resuspended with gentle shaking of the tube. A single drop of urine sediment is placed on a glass slide and examined under a microscope. Although automated microscopic platforms have been developed to identify cells and particles in urine, the diagnostic yield may be substantially greater when it is performed by a clinician trained in urine microscopy.[39,40] Urine microscopy can primarily be used to evaluate cellular structures (**Table 6**), casts (**Table 7**), and crystals (**Table 8**). While routine use of urine microscopy is not anticipated in non-nephrology settings, a basic understanding of the impact of urine microscopy in clinical diagnosis and management of patients is important.

SUMMARY

Urinalysis is a powerful tool and can be integral to the clinical evaluation of patients with kidney diseases (**Tables 9** and **10**). Correct acquisition of the sample and interpretation of findings within the context of the clinical situation can not only provide valuable information to internists but also guide next steps in diagnostic and therapeutic interventions.

CLINICS CARE POINTS

- Urinalysis should be performed in patients with acute or chronic kidney injury, evidence of kidney stones, change in urine appearance, or urinary symptoms.
- Proper collection and handling of urine specimens is key to reliability of findings.
- Patients with hypertension, diabetes mellitus, or cardiovascular disease should be screened for proteinuria.
- The presence and degree of proteinuria (especially albuminuria) is important for chronic kidney disease (CKD) staging and prognostication and should be monitored at regular intervals for patients with proteinuric CKD.
- Glucosuria in the absence of hyperglycemia suggests proximal tubular dysfunction, which can be seen in multiple myeloma and cast nephropathies, or due to exposure to certain drugs such as sodium/glucose cotransporter-2 inhibitors.
- Unexplained persistent proteinuria or hematuria, and nephrotic range proteinuria, warrant further investigation including consideration of referral to nephrology.

DISCLOSURE

The authors have nothing to disclose.

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